



Clinical trial results:

Estrategias para mejorar la eficacia y seguridad del tratamiento con Simvastatina en la Fase Aguda del Ictus Isquémico: STARS trial.

Improving Safety and Efficacy of Simvastatin Treatment for the Acute Phase of Ischemic Stroke: STARS trial.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-005868-26 |
| Trial protocol | ES |
| Global end of trial date | 10 March 2014 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 20 October 2021 |
| First version publication date | 20 October 2021 |
| Summary attachment (see zip file) | Stroke2016 Montaner (STROKEAHA.116.014600.pdf) |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | stars07 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01073007 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | VHIR |
| Sponsor organisation address | Passeig Vall Hebron 119-129, Barcelona, Spain, 08035 |
| Public contact | Joaquin Lopez-Soriano, VHIR, joaquin.lopez.soriano@vhir.org |
| Scientific contact | Joan Montaner, VHIR, +34 932746766, joan.montaner@vhir.org |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 10 March 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 March 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Demostrar que en la fase aguda del ictus isquémico el tratamiento con Simvastatina administrado en las primeras 12h del inicio de los síntomas mejora la situación neurológica y funcional del paciente valorado a los 7 días y tercer mes del inicio del tratamiento.

[To demonstrate that in the acute phase of ischemic stroke, Simvastatin given within 12 hours of stroke onset improves neurological and functional status evaluated at day seven (or at discharge if this occurs before day 7) and at three months respectively].

Protection of trial subjects:

Neurological deterioration (increase of the NIHSS ≥ 4 points) and major neurological improvement (NIHSS score of 0 or decrease in the NIHSS score, ≥ 8) were assessed at 7 days.

Background therapy:

Intravenous tPA.

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 03 March 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Spain: 104 |
| Worldwide total number of subjects | 104 |
| EEA total number of subjects | 104 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 20 |

| | |
|---------------------|----|
| From 65 to 84 years | 84 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|----------------------------|-----|
| Number of subjects started | 104 |
|----------------------------|-----|

| | |
|------------------------------|-----|
| Number of subjects completed | 104 |
|------------------------------|-----|

Period 1

| | |
|----------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
|----------------|--------------------------------|

| | |
|------------------------------|-----|
| Is this the baseline period? | Yes |
|------------------------------|-----|

| | |
|-------------------|-------------------------|
| Allocation method | Randomised - controlled |
|-------------------|-------------------------|

| | |
|---------------|--------------|
| Blinding used | Double blind |
|---------------|--------------|

| | |
|---------------|-----------------------|
| Roles blinded | Subject, Investigator |
|---------------|-----------------------|

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

| | |
|----------|-----------------|
| Arm type | No intervention |
|----------|-----------------|

No investigational medicinal product assigned in this arm

| | |
|------------------|-------------|
| Arm title | Simvastatin |
|------------------|-------------|

Arm description: -

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|-------------|
| Investigational medicinal product name | Simvastatin |
|--|-------------|

| | |
|--|--|
| Investigational medicinal product code | |
|--|--|

| | |
|------------|--|
| Other name | |
|------------|--|

| | |
|----------------------|------------------------|
| Pharmaceutical forms | Solution for injection |
|----------------------|------------------------|

| | |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

40 mg once daily for 90 days

| Number of subjects in period 1 | Placebo | Simvastatin |
|--------------------------------|---------|-------------|
| Started | 54 | 50 |
| Completed | 50 | 48 |
| Not completed | 4 | 2 |
| Lost to follow-up | 4 | 2 |

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|------------------------------|---------------|-------|--|
| Number of subjects | 104 | 104 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 20 | 20 | |
| From 65-84 years | 84 | 84 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 74 | | |
| inter-quartile range (Q1-Q3) | 62.5 to 82 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 48 | 48 | |
| Male | 56 | 56 | |

End points

End points reporting groups

| | |
|-----------------------------------|--------------------|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Simvastatin |
| Reporting group description: - | |
| Subject analysis set title | Complete treatment |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Rankin Scale score | |

Primary: Rankin scale

| | |
|-----------------------------|--------------|
| End point title | Rankin scale |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| At the end of the treatment | |

| End point values | Placebo | Simvastatin | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 48 | | |
| Units: unit(s) | | | | |
| number (not applicable) | | | | |
| Under 2 | 35 | 33 | | |

Statistical analyses

| | |
|---|-----------------------|
| Statistical analysis title | Rankin scale |
| Comparison groups | Placebo v Simvastatin |
| Number of subjects included in analysis | 98 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | = 0.98 |
| Method | t-test, 1-sided |

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All the study

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Total adverse events |
|-----------------------|----------------------|

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: All the reported adverse events were considered as serious. Non-serious events were not reported in the final publication (no additional data available)

| Serious adverse events | Total adverse events | | |
|---|----------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 104 (11.54%) | | |
| number of deaths (all causes) | 5 | | |
| number of deaths resulting from adverse events | 0 | | |
| Cardiac disorders | | | |
| Heart failure | | | |
| subjects affected / exposed | 2 / 104 (1.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angor | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Malignant edema | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Neurological deterioration | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Symptomatic intracerebral hemorrhage | | | |
| subjects affected / exposed | 2 / 104 (1.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Status epilepticus | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Meningitis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Delirium | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| CRA branch occlusion | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory infection | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 2 / 104 (1.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchial aspiration procedure | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 104 (1.92%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 104 (0.96%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| | | | |
|---|----------------------|--|--|
| Non-serious adverse events | Total adverse events | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 104 (0.00%) | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| Because of the low recruitment, the STARS trial was underpowered to detect differences in simvastatin efficacy. |
|---|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/27758944>